

## REMARKS

### The invention

The invention features methods for treating a patient who has a neoplasm, or for inhibiting the development of a neoplasm in a patient, by administering a combination of compounds to the patient.

### The Office Action

Claims 2, 5-15, 17-26, 28-29, and 40-62 were pending at the time of the Office Action. Claims 2, 5-15, 17-26, 28-29, and 40-62 stand rejected under 35 U.S.C. § 112, first paragraph, for insufficient scope of enablement. Claims 2, 5, 7-9, 28-29, and 40-62 stand rejected for obviousness-type double patenting in view of claims 1-24 and 35 of U.S. Patent No. 6,569,853 (“the ‘853 patent”), and further in view of claims 1-13 of U.S. Patent No. 6,846,816 (“the ‘816 patent”). Claims 2, 7-9, 11, 17-26, 28-29, and 40-62 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dwivedi et al. (J. Pharmacol. Exp. Therapeutics, 291:688-704, 1999) in view of Makulu et al. (Am. Soc. Pharmacol. Exp. Therapeutics, 16:105, 1974), and further in view of Windholz et al. (The Merck Index (1983) Tenth Edition, page 183, abstract 1308). Applicants address each of these rejections in turn below.

### Claim amendments

Claims 11, 17-20, 22-25, 40, 45-48, 50-53, 55-57, and 59-62 have been canceled. Claims 2, 10, and 28 have been amended to read only on treatment of lung cancer. Claims 12, 21, 41, 49, and 58 have been amended to correct claim dependencies in view of canceled or amended claims. Claim 26 has been amended to recite “said first compound” and “said second compound” in order to correct antecedent basis. Support for these amendments may be found, for example, on page 15, lines 25-28 and page 43, line 25 to page 44, line 3 of the specification as filed. No new matter has been added by the present amendments.

As all amendments made by Applicants reduce the issues for appeal, Applicants respectfully request that these amendments be entered.

### Rejections under 35 U.S.C. § 112, first paragraph

Claims 2, 5-15, 17-26, 28-29, and 40-62 stand rejected under 35 U.S.C. § 112, first paragraph, for insufficient scope of enablement. The Office states on page 4:

[T]he specification, while being enabling for treating a neoplasm with a composition comprising components formula (I) and formula (II), wherein the neoplasm is lung cancer, does not reasonably provide enablement for the composition comprising formula (I) and formula (II) to treat other types of neoplasm or the addition of a third agent as disclosed in claims 17, 18, 45 and 46.

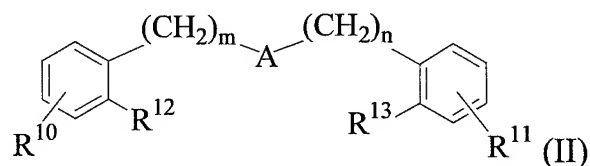
Applicants respectfully disagree that the specification is not enabling for neoplasms other than lung cancer or for the addition of a third agent as recited in claims 17, 18, 45, and

46. However, in order to expedite prosecution, Applicants have amended claims 2, 10, and 28 to read only on treating or inhibiting lung cancer. Applicants have also canceled claims 17, 18, 45, and 46 so as not to claim treatment with a third agent as recited in these claims. In addition, claims 11, 19-20, 22-25, 40, 47-48, 50-53, 55-57, and 59-62 have been canceled, and claims 12, 21, 41, 49, and 58 have been amended to correct claim dependencies in view of canceled or amended claims. The claims as presently amended are limited to subject matter that the Office has indicated is enabled by the specification. Therefore, the enablement rejection should be withdrawn.

#### Rejections for obviousness-type double patenting

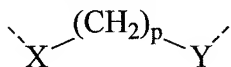
Claims 2, 5, 7-9, 28-29, and 40-62 stand rejected for obviousness-type double patenting in view of claims 1-24 and 35 of the '853 patent, and further in view of claims 1-13 of the '816 patent.

Applicants respectfully note that this rejection is based on an error, namely, the Examiner's erroneous belief that the claims of the present invention are generic to all that is recited in the claims of the '853 patent and the '816 patent. Turning first to the rejection based on the '853 patent, which is directed to combinations of chlorpromazine and pentamidine, Applicants draw the Office's attention to formula (II) of the present specification, reproduced below:



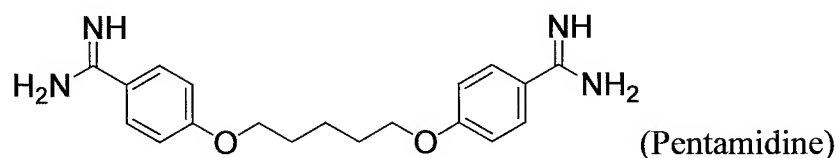
Independent claims 2 and 28 each recite three possible sets of limitations for compounds of formula (II), any of which may apply. The first set of limitations (“limitation set A”) begins as follows:

...wherein A is



each of X and Y is, independently, O or NH,  
 p is an integer between 2 and 6, inclusive,  
 each of m and n is, independently, an integer between 0 and 2, inclusive, **wherein the sum of m and n is greater than 0...**[emphasis added]

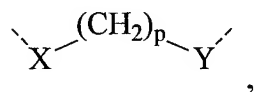
The fact that the sum of m and n is greater than zero necessarily implies that either m or n must be positive, i.e., there must be at least one methylene group between group A and either aryl ring. Pentamidine, shown below, does not satisfy this limitation.



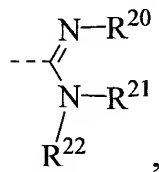
Note that each oxygen in pentamidine is covalently bonded directly to an aryl ring without any intervening methylene groups. Thus, limitation set A clearly excludes pentamidine.

Likewise, the other two sets of limitations for compounds of formula (II) recited in claims 2 and 28 also exclude pentamidine. The second set of limitations (“limitation set B”) begins as follows:

or A is



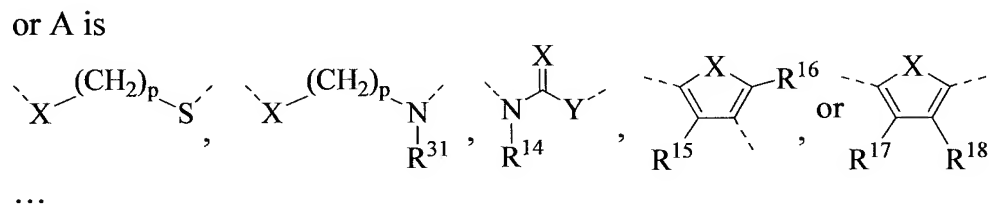
each of X and Y is, independently, O or NH,  
 p is an integer between 2 and 6, inclusive,  
 each of m and n is 0, and  
 each of R<sup>10</sup> and R<sup>11</sup> is, independently, selected from the group  
 represented by



wherein R<sup>21</sup> is C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>8</sub> cycloalkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy  
 C<sub>1</sub>-C<sub>6</sub> alkyl, hydroxy C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkylamino C<sub>1</sub>-C<sub>6</sub>  
 alkyl, amino C<sub>1</sub>-C<sub>6</sub> alkyl, or C<sub>6</sub>-C<sub>18</sub> aryl...[emphasis added]

In pentamidine, each of R<sup>20</sup>, R<sup>21</sup>, and R<sup>22</sup> is H; however, according to limitation set B, R<sup>21</sup>  
 cannot be H. Thus, limitation set B excludes pentamidine.

Similarly, the third set of limitations (“limitation set C”) begins as follows:

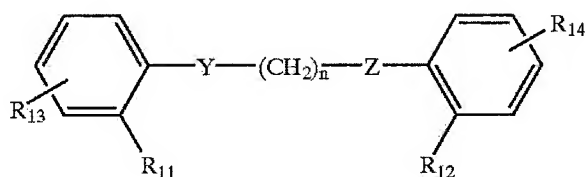


Limitation set C does not allow for two oxygens that are each covalently bonded directly  
 to an aryl ring, as occurs in pentamidine.

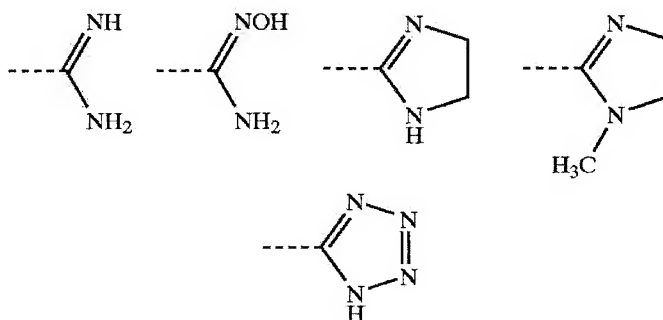
It is clear from the above analysis that claims 2 and 28, as well as dependent  
 claims thereof, do not encompass pentamidine, and therefore do not read on any of the  
 claims of the ‘853 patent.

A similar analysis shows that the present claims also do not read on any of the  
 claims of the ‘816 patent, which is directed to combinations of chlorpromazine analogs  
 and pentamidine analogs. Briefly, formula (II) of the ‘816 patent, along with the

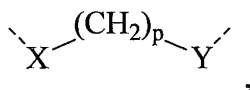
corresponding limitations recited in independent claims 1 and 13 of that patent, are shown below:



or a pharmaceutically acceptable salt thereof, wherein each of Y and Z is, independently, O or N; each of  $R_{11}$  and  $R_{12}$  is, independently, H, Cl, Br, OH,  $OCH_3$ ,  $OCF_3$ ,  $NO_2$ , and  $NH_2$ ; n is an integer between 2 and 6, inclusive; and each of  $R_{13}$  and  $R_{14}$  is, independently, selected from the group consisting of:



As before, limitation set A of the present claims clearly does not read on any of the pentamidine analogs of the '816 patent, because limitation set A requires that there be at least one intervening methylene group between group X or Y and the corresponding aryl ring. Limitation set B does not allow for any of the five possibilities shown for  $R_{13}$  and  $R_{14}$  of the '816 patent. Finally, limitation set C does not allow for A to be



wherein each of X and Y is, independently, O or N, as the claims of the '816 patent require. Thus, the present claims do not read on any of the claims of the '816 patent. Accordingly, the rejection for obviousness-type double patenting should be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 2, 7-9, 11, 17-26, 28-29, and 40-62 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Dwivedi et al. in view of Makulu et al., and further in view of Windholz et al. In maintaining this rejection from the first Office Action, the Office states on page 6: "Applicants' claims 2 and 28 containing component (b), formula (II) still reads on pentamidine." Applicants respectfully disagree. As presented above in reference to the rejections for obviousness-type double patenting, claims 2 and 28 do not read on pentamidine. In addition, claim 10 does not read on pentamidine, in view of the amendments made in Applicants' reply filed on August 9, 2005. Therefore, there is nothing in any of the cited references that would have led one to the combinations of compounds recited in any of the claims. In view of the foregoing, the rejection under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

Applicants submit that the claims are now in condition for allowance and such action is respectfully requested. Enclosed is a Petition to extend the period for replying to the Office Action for one month, to and including February 24, 2006. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: Feb. 22, 2006



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